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ORIGINAL ARTICLE

Upregulation of microRNA Processing Enzymes Drosha and Dicer in Gestational Diabetes Mellitus

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Abstract

MicroRNAs (miRNAs) have been shown to play important roles in diverse cellular processes and linked to variety of disorders. Dicer and Drosha are two major enzymes in the miRNA biogenesis process. DGCR8 is the assistant of Drosha in the microprocessor complex. In this study, we evaluated the mRNA expression profiles of major miRNA processing machinery Drosha, Dicer, and DGCR8 in gestational diabetes mellitus (GDM), pregnant and healthy women. Our findings indicate that the expression levels of Drosha, Dicer and DGCR8 were upregulated in both pregnant and GDM patients compared to the control group. However, Drosha and Dicer were upregulated more than pregnant group. In conclusion, we detected dysregulation of Drosha, Dicer and DGCR8 expression in pregnant and GDM patients when compared to healthy control participants. Therefore, we favor the hypothesis that miRNAs are involved in the development of GDM.

Keywords

Drosha, Dicer, DGCR8, Gestational Diabetes Mellitus, microRNA, pregnancy

History

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Introduction

Gestational diabetes mellitus (GDM) is characterized as glucose intolerance that begins during pregnancy. The American Diabetes Association has defined GDM as diabetes diagnosed during pregnancy that is not clearly overt diabetes [1,2]. It is the most common endocrine disorder in pregnancy and affects from 1.4% to 14% of all pregnant women depending on the diagnostic criteria and population characteristics [3]. This condition is associated with unfavorable pregnancy outcomes, including fetal macrosomia, stillbirth, neonatal metabolic disturbances, and related complications [4].

MicroRNAs (miRNAs) are tiny endogenous single-stranded RNAs that regulate the expression of several target genes post-transcriptionally. miRNAs function by binding to the 3′-untranslated region (UTR) of their target genes with partial complementarity. Up to present, more than 1000 human miRNAs have been recognized, that each of them potentially controls hundreds of target genes. It has been clarified that these miRNAs act as important gene regulators to control several physiological events, including metabolic disorders such as diabetes [5,6]. Transcription of miRNAs occurs through RNA polymerase II and following processing is mediated by the nuclear ribonuclease III (RNase III) enzyme Drosha and its co-activator, DGCR8 to produce precursor miRNAs (70–100 nucleotides) [7]. After translocation to the cytoplasm, further cleavage occurs via another RNase III enzyme, Dicer, to form the mature miRNA [8]. Therefore, Drosha, DGCR8, and Dicer are key components of miRNA machinery.

Recently, some common and specific miRNAs have been identified in GDM patients [9]. Moreover, it has been reported that serum miRNAs are differentially expressed in GDM women in comparison to the controls [10].

Considering all the facts that miRNAs are differentially expressed in GDM patients, we aimed to investigate expression of major miRNA machinery components including Drosha, DGCR8, and Dicer in GDM, pregnant and healthy women.

Methods and patients

Ethics statement

Human Research Ethics Committees from the Ardabil University of Medical Sciences approved this study. Written informed consent was given by all participants.

All participants had not any infection or other disorders at the time of sample collection; the demographic and laboratory features of healthy controls, pregnant and GDM patients are shown in Table 1. Exclusion criteria included recent episodes of ketoacidosis, active nephropathy, proliferative retinopathy, diabetic foot, high HDL (high-density lipoprotein) levels and diagnosed cardiovascular diseases.

Blood samples from pregnant individuals and GDM patients were obtained during clinical diagnosis. Blood analysis from healthy donors was also performed with written informed consent.

Blood extraction was always performed in the early morning by trained phlebotomists at Obstetrics and Gynecology Clinic of Alavi Hospital. In all cases, under sterile conditions 10 ml of peripheral blood were collected in EDTA, anti-coagulated tubes by venipuncture.

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